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Steven J. Barbee, Ph.D.
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201-14277

Christine Todd Whitman
Administrator, US EPA
PO Box 1473
Merrifield, VA 22116

January 7, 2003

Re: Chemical Right-to-Know HPV Chemical Challenge Program

Dear Administrator Whitman:

On behalf of Arch Chemicals, Inc. (Arch), I am pleased to submit the test plan and robust summaries for 2-chloropyridine (CAS No. – 109-09-1).

Enclosed with this letter are two copies of the test plan and robust summaries – one in hard copy and one on computer diskette in Microsoft Word format. The HPV registration number for Arch is

Arch understands that this information will be posted on the Internet for comments for a period of 120 days. Please forward comments to me at the above address.

Sincerely yours,

Steven J. Barbee, Ph.D., DABT, CIH

201-14277A

HIGH PRODUCTION VOLUME (HPV) CHALLENGE PROGRAM

TEST PLAN

FOR

2-CHLOROPYRIDINE

CAS NO. – 109-09-1

PREPARED BY:

ARCH CHEMICALS, INC.

January 7, 2003

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OVERVIEW

Arch Chemicals, Inc. (Arch) hereby submits for review and public comment the test plan for 2-chloropyridine (2-PCl; CAS # 109-09-1) under the Environmental Protection Agency's High Production Volume Chemical Challenge Program. It is the intent of Arch to use existing data, data proposed under the test plan and estimated values using predictive computer models acceptable to EPA to adequately fulfill the Screening Information Data Set (SIDS) for the physical/chemical endpoints, environmental fate, ecotoxicity and human health-related toxicology.

2-PCl is a colorless, oily liquid used as an intermediate in synthetic organic, pharmaceutical and agricultural chemical manufacture. It is a key intermediate in the manufacture of pyrithione-based biocides for use in cosmetics and various pharmaceutical products. It is also used as a starting material in the production of the antihistamine drug, pheniramine and the antiarrhythmic drug, diisopyramide. This chemical is not sold to the individual consumer. Its uses are in the industrial workplace where exposures are tightly controlled.

TEST PLAN SUMMARY

2-Chloropyridine CAS # 109-09-1	Information	OECD Study	Other	Estimation	GLP	Acceptable	New Testing Required
STUDY	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
PHYSICAL-CHEMICAL DATA							
Melting Point	Y	-	-	Y	N	Y	N
Boiling Point	Y	-	-	Y	N	Y	N
Vapor Pressure	Y	-	-	Y	N	Y	N
Partition Coefficient	Y	-	-	Y	N	Y	N
Water Solubility	Y	-	-	Y	N	Y	N
ENVIRONMENTAL FATE DATA							
Photodegradation	Y	-	-	Y	N	Y	N
Stability in Water	N	-	-	-	-	-	N
Biodegradation	Y	N	Y	N	N	Y	N
Transport between Environmental Compartments (Fugacity)	Y	-	-	Y	N	Y	N
ECOTOXICOLOGICAL DATA							
Acute Toxicity to Fish	Y	-	-	Y	N	Y	N
Acute Toxicity to Aquatic Invertebrates	Y	-	-	Y	N	Y	N
Toxicity to Aquatic Plants	Y	-	-	Y	N	Y	N
MAMMALIAN TOXICOLOGICAL DATA							
Acute Toxicity	Y	N	-	-	N	Y	N
Repeated Dose Toxicity	N	-	-	-	-	-	Y
Genetic Toxicity							
Mutation	Y	N	Y	-	N	Y	N
Chromosomal Aberration	Y	N	Y	-	N	Y	N
Developmental Toxicity	N	-	-	-	-	-	Y
Toxicity to Reproduction	N	-	-	-	-	-	Y

TEST PLAN DESCRIPTION FOR EACH SIDS ENDPOINT

A. Physical/Chemical Endpoints

Melting Point – A value for this endpoint was obtained using a computer estimation model (EPIWIN, Version 3.10.).

Boiling Point – A value for this endpoint was obtained using a computer estimation model (EPIWIN, Version 3.10.) and from a reliable reference text. The entry from the reference text (Sax and Lewis, 1987) is the preferred value.

Vapor Pressure – A value for this endpoint was obtained using a computer estimation model (EPIWIN, Version 3.10.).

Partition Coefficient – A value for this endpoint was obtained using a computer estimation model (EPIWIN, Version 3.10.) and from a reliable reference text. The entry from the reference text (Hansch et al., 1995) is the preferred value.

Water Solubility – A value for this endpoint was obtained using a computer estimation model (EPIWIN, Version 3.10.) and from a reliable reference text. The entry from the reference text (CRC Handbook of Chemistry and Physics, 1995) is the preferred value.

Conclusion – All endpoints have been satisfied by the utilization of data obtained from the various physical/chemical data modeling programs or reliable reference texts as referenced above. The results from the utilization of these computer modeling programs are recognized by EPA as acceptable in lieu of actual data or values obtained from literature references. Thus, no new testing is needed in the area of physical/chemical properties.

B. Environmental Fate Endpoints

Photodegradation – A value for this endpoint was obtained using a computer estimation model (EPIWIN, Version 3.10.).

Stability in Water – Although hydrolysis can not be predicted using a computer estimation model, 2-chloropyridine does not have a site in which the water molecule or hydroxide ion can displace an atom or group of atoms. Chemical hydrolysis at a pH normally found in the environment, i.e. 5 to 9, can be important for a variety of chemicals that have functional groups that are potentially hydrolysable, such as amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters.

Biodegradation – This endpoint was satisfied using studies to assess degradation in both anaerobic (3 studies) and aerobic (2 studies) systems. There was not one study that could be singled out as the key study. They all indicate that 2-

chloropyridine is resistant to biodegradation. In the aerobic system 1-10% was degraded in 24-64 days. In the anaerobic system no significant biodegradation was detected. Therefore, the 5 studies should be taken as a package to indicate that 2-chloropyridine is resistant to biodegradation.

Fugacity – A value for this endpoint was obtained using the EPIWIN Level III portioning computer estimation model (EPIWIN, Version 3.10.).

Conclusion – All endpoints have been satisfied using actual data, through the use of EPA-acceptable estimation models, or, in the case of stability in water, scientific judgment to support the position for testing requirements. No additional testing is needed in the area of environmental fate.

C. Ecotoxicity Endpoints

Acute Toxicity to Fish – A value for this endpoint was obtained using a computer program for estimating the ecotoxicity of industrial chemicals based on structure-activity relationships (Nabholz et al., 2001).

Acute Toxicity to Aquatic Invertebrates – A value for this endpoint was obtained using a computer program for estimating the ecotoxicity of industrial chemicals based on structure-activity relationships (Nabholz et al., 2001).

Toxicity to Aquatic Plants – A value for this endpoint was obtained using a computer program for estimating the ecotoxicity of industrial chemicals based on structure-activity relationships (Nabholz et al., 2001).

Conclusion – All endpoints have been satisfied through the use of EPA-acceptable estimation models. No additional testing is needed in the area of ecotoxicity.

D. Mammalian Toxicological Endpoints

Acute Toxicity – The studies that satisfy this endpoint were conducted prior to introduction of GLP. However, all studies (oral LD_{50}, dermal LD_{50} and inhalation LC_{50}) to define the acute toxicological profile were conducted in accordance with currently accepted scientific principles and are considered reliable. Two studies were conducted to define the acute dermal toxicity. The study by Gehring et al. (1967) is the key study because it determined a specific dermal LD_{50} value contrasted with the study by Wazeter (1964) in which the LD_{50} was characterized as less than an observed value. Two studies were conducted to define the acute inhalation toxicity. The study by Gehring et al. (1967) is the key study because it defined the LC_{50} value between two concentrations contrasted with the study by Wazeter (1964) in which the LC_{50} was characterized as less than an observed value.

Repeat Dose Toxicity – This endpoint has not been satisfied. A study will be conducted to address this endpoint and will conform to OECD guidelines (OECD 407) and will be conducted according to GLP guidelines.

Genetic Toxicity

Mutation (bacterial) – This endpoint has been satisfied with an Ames/*Salmonella* reverse mutation bacterial assay using strains TA97, TA98, TA100 and TA102 of *Salmonella typhimurium.* This study is reliable and is comparable to a guideline study (OECD 471).

Mutation (mammalian, *in vitro*) – Since the Ames assay indicates that 2-chloropyridine is positive, the OECD SIDS guidelines suggest a mammalian gene mutation assay be conducted. This endpoint was satisfied with a forward mutation assay using heterozygous L5178Y $TK^{+/-}$ -3.7.2C mouse lymphoma cells. This study is reliable and was conducted according to accepted scientific principles.

Chromosomal aberration (mammalian, *in vitro*) – This endpoint was evaluated as a component of the study to assess point mutation in heterozygous L5178Y $TK^{+/-}$ -3.7.2C mouse lymphoma cells. The cells were evaluated for chromosomal aberrations and micronuclei.

Developmental Toxicity – This endpoint has not been satisfied. A study will be conducted to address this endpoint and will conform to OECD guidelines (OECD 421) and will be conducted according to GLP guidelines.

Reproductive Toxicity – This endpoint has not been satisfied. A study will be conducted to address this endpoint and will conform to OECD guidelines (OECD 421) and will be conducted according to GLP guidelines.

Conclusion – The endpoints for acute toxicity and genetic toxicity have been satisfied with data from studies that were conducted utilizing methods that are similar to established guidelines and are scientifically appropriate. The endpoints of repeat dose toxicity, reproductive toxicity and developmental toxicity have not been satisfied. Studies will be conducted to supply data for these endpoints and they will be conducted according to OECD guidelines and GLP assurances.

SIDS DATA SUMMARY

Data to assess the various physicochemical properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility) for 2-chloropyridine were obtained from EPA-acceptable computer estimation modeling programs found in EPIWIN. These data indicate that 2-chloropyridine is a liquid at room temperature with a low vapor pressure. It has a low estimated octanol to water partition coefficient and is moderately soluble in water. The use of these modeled data meet the requirements of the various endpoints and thus there is no need for any additional testing to determine physicochemical properties.

Data to address endpoints for environmental fate of photodegradation, biodegradation and fugacity were obtained from actual studies or EPA-acceptable computer estimation modeling programs found in EPIWIN. As a result of its solubility in water and relatively low volatility, fugacity estimations predict that 2-chloropyridine will distribute primarily to soil and water. Computer modeling predicts that 2-PCl will slowly degrade in the atmosphere. Actual testing using aerobic and anaerobic systems indicates that 2-PCl is resistant to biodegradation. The computer modeling program can not estimate the rate constants for aqueous base/acid-catalyzed hydrolysis. Although hydrolysis cannot be predicted using a computer estimation model, 2-chloropyridine does not have a site in which the water molecule or hydroxide ion can displace an atom or group of atoms. Chemical hydrolysis at a pH normally found in the environment, i.e. 5 to 9, can be important for a variety of chemicals that have functional groups that are potentially hydrolysable, such as amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters. It is the position of Arch Chemicals that data for this endpoint is not necessary since this chemical does not possess a structure that is hydrolysable. The judgment is that 2-PCl would be resistant to acid/base-catalyzed hydrolysis.

The data for aquatic toxicity endpoints were obtained from EPA-acceptable computer estimation modeling programs found in ECOSAR (Nabholz et al., 2001). 2-Chloropyridine is of moderate toxicity to fish, daphnids and algae. The LC_{50} to fish (96 hours) and *Daphnia* (48 hours) is 277 mg/l and 286 mg/l, respectively. The EC_{50} (96 hours) to algae is 173 mg/l.

The data to determine acute toxicity and genetic toxicity are from studies that were conducted according to acceptable scientific methodology. The inhalation LC_{50} (4 hours) is between 100 and 250 ppm. The oral LD_{50} and dermal LD_{50} are 342 mg/kg and 64 mg/kg, respectively. 2-Chloropyridine induces mutations in two separate *in vitro* systems, the Ames/*Salmonella* assay (Claxton et al., 1987) and in a mammalian assay using mouse lymphoma (L5178Y) cells (Dearfield et al., 1993). Dearfield et al. (1993) also found 2-chloropyridine to be clastogenic as demonstrated by increases in chromosome aberrations and micronuclei. Based on the results of the mutagenicity assays, 2-chloropyridine is classified as a mutagen.

EVALUATION OF DATA FOR QUALITY AND ACCEPTABILITY

The collected data were reviewed for quality and acceptability following the systematic approach described by Klimisch et al. (1997). The codification described by Klimisch specifies four categories of reliability for describing data adequacy. They are:

1. Reliable without restriction: Includes studies or data complying with Good Laboratory Practices (GLP) procedures, or with valid and/or internationally accepted testing guidelines, or in which the test parameters are documented and comparable to these guidelines.

2. Reliable with restrictions: Includes studies or data in which test parameters are documented but vary slightly from testing guidelines.

3. Not reliable: Includes studies or data in which there are interferences, or that use non-relevant organisms or exposure routes, or which were carried out using unacceptable methods, or where documentation is insufficient.

4. Not assignable: Includes studies or data in which insufficient detail is reported to assign a rating, e.g., listed in abstracts or secondary literature.

REFERENCES

1. EPIWIN, (EPI Suite™ v.3.10). Downloadable at http://www.epa.gov/oppt/exposure/docs/episuitedl.htm ©2000 U.S. Environmental Protection Agency.

2. Klimisch, H.-J., Andreae, M. and Tillman, U. 1997. A Systematic Approach for Evaluating the Quality of Experimental Toxicological and Ecotoxicological Data. Regul. Toxicol. Pharmacol. 25, 1-5.

3. Nabholz, J. V., Cash, G., Meylan, W. M. and Howard, P. H. 2001. ECOSAR: A Computer Program for Estimating the Ecotoxicity of Industrial Chemicals Based on Structure Activity Relationships, Version 0.99g. Washington, DC: Risk Assessment Division, Office of Pollution Prevention and Toxics, United States Environmental Protection Agency. Available from EPA web page at http://www.epa.gov/oppt/newchems/21ecosar.htm or http://www.epa.gov/oppt/exposure/docs/episuitedl.htm

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5. Hansch, C., Leo, A. and Hoekman, D. 1995. Exploring QSAR: Hydrophobic, Electronic and Steric Constants. American Chemical Society. ACS Professional Reference Book, ACS, Washington, DC.

6. Lide, D. R. and Frederikse, H. P. R., eds. CRC Handbook of Chemistry and Physics, 75th ed. CRC Press, Boca Raton, FL. 1995.

7. Wazeter, F. X. 1964. Acute Toxicity Studies in Rats and Rabbits. Report # 122-003. International Research and Development Corporation, Mattawan, MI.

8. Gehring, P. J., Torkelson, T. R. and Oyen, F. 1967. A Comparison of the Lethality of Chlorinated Pyridines and a Study of the Acute Toxicity of 2-Chloropyridine. Toxicol. Appl. Pharmacol. 11, 361-371.

General Information

CAS Number: 109-09-1
Common Name: 2-Chloropyridine

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II. Physical-Chemical Data

A. Melting Point

Test Substance

Identity: 2-Chloropyridine
Remarks: Mean or weighted melting point

Method

Method: Estimation
Remarks: None

Results

Melting Point Value: -12.6°C
Remarks: None

Reference MPBPWIN v1.40 (EPI Suite™ v.3.10). Downloadable at http://www.epa.gov/oppt/exposure/docs/episuitedl.htm ©2000 U.S. Environmental Protection Agency.

Other

B. Boiling Point

Entry 1 of 2

Test Substance

Identity:	2-Chloropyridine
Remarks:	None

Method

Method:	Estimation
Remarks:	Adapted from Stein & Brown method

Results

Boiling Point Value:	150.07°C
Remarks:	None

Reference MPBPWIN v1.40 (EPI Suite™ v.3.10). Downloadable at http://www.epa.gov/oppt/exposure/docs/episuitedl.htm ©2000 U.S. Environmental Protection Agency.

Other

Entry 2 of 2 for Boiling Point

Test Substance

Identity:	2-Chloropyridine
Purity:	Not stated
Remarks:	None

Method

Method:	Not stated
GLP:	Not stated
Year:	Not stated
Remarks:	None

Results

Boiling Point Value:	170^{o}C
Remarks:	None

Conclusions The boiling point was provided in a reliable resource book. The endpoint has been adequately characterized.

Data Quality

Reliability:	2D
Remarks:	Reliable with restrictions; endpoint was provided in a reliable reference text.

Reference Sax, N. I. and R. J. Lewis, Sr. 1987. Hazardous Chemicals Desk Reference. Pp. 332-333. Van Nostrand Reinhold Co., NY, NY.

Other

C. Vapor Pressure

Test Substance

Identity:	2-Chloropyridine
Remarks:	None

Method

Method:	Estimation
Remarks:	Mean of Antoine and Grain methods

Results

Vapor PressureValue:	1.56 mmHg @ 25^{o}C
Remarks:	None

Reference MPBPWIN v1.40 (EPI Suite™ v.3.10). Downloadable at http://www.epa.gov/oppt/exposure/docs/episuitedl.htm ©2000 U.S. Environmental Protection Agency.

Other

D. Partition Coefficient – Entry 1 of 2

Test Substance

Identity:	2-Chloropyridine
Remarks:	None

Method

Method:	Estimation
Remarks:	None

Results

K_{ow}:	1.45
Remarks:	None

Reference KOWWIN v.1.66. (EPI Suite™ v.3.10). Downloadable at http://www.epa.gov/oppt/exposure/docs/episuitedl.htm ©2000 U.S. Environmental Protection Agency.

Other

Entry 2 of 2 for Partition Coefficient

Test Substance

Identity:	2-Chloropyridine
Purity:	Not stated
Remarks:	None

Method

Method:	Not stated
GLP:	Not stated
Year:	Not stated
Remarks:	None

Results

K_{ow}:	1.22
Temperature:	Not stated
Remarks:	None

Conclusions The partition coefficient was provided in a reliable resource book. The endpoint has been adequately characterized.

Data Quality:

Reliability:	2D
Remarks:	Reliable with restrictions; information provided in a reliable reference text.

Reference Hansch, C., Leo, A. and Hoekman, D. 1995. Exploring QSAR: Hydrophobic, Electronic and Steric Constants. American Chemical Society. ACS Professional Reference Book, ACS, Washington, DC.

Other

E. Water Solubility

Entry 1 of 2

Test Substance

Identity:	2-Chloropyridine
Remarks:	None

Method

Method:	Estimation
Remarks:	None

Results

Value:	9,609 mg/l
Temperature:	25^{o}C
Remarks:	A K_{ow} of 1.22 was used in this estimation.

Reference WSKOW v1.40 (EPI Suite™ v.3.10). Downloadable at http://www.epa.gov/oppt/exposure/docs/episuitedl.htm ©2000 U.S. Environmental Protection Agency.

Other

Entry 2 of 2 for Water Solubility

Test Substance

Identity:	2-Chloropyridine
Purity:	Not stated
Remarks:	None

Method

Method:	Not stated
GLP:	Not stated
Year:	Not stated
Remarks:	None

Results

Value:	2,000 mg/l
Temperature:	25^{o}C
Remarks:	None

Conclusions The water solubility was provided in a reliable resource book. The endpoint has been adequately characterized.

Data Quality

Reliability:	2D
Remarks:	Reliable with restrictions; information provided in a reliable reference text.

Reference Lide, D. R. and Frederikse, H. P. R., eds. CRC Handbook of Chemistry and Physics, 75th ed. CRC Press, Boca Raton, FL. 1995.

Other

III. Environmental Fate Endpoints

A. Photodegradation

Test Substance

Identity:	2-Chloropyridine
Remarks:	None

Method

Method:	Estimation
Test type:	Atmospheric oxidation
Remarks:	None

Results

Hydroxyl radicals reaction:	
OH Rate Constant:	0.2603 x 10^{-12} cm^3/molecule-sec
Half-life:	41.094 days (12-hr day; 1.5 x 10^6 OH/cm^3
Temperature:	25^0C
Ozone reaction:	No ozone reaction estimation was noted.
Remarks:	None

Conclusions The material is expected to slowly degrade in the atmosphere.

Reference AopWin v1.90. (EPI Suite™ v.3.10). Downloadable at http://www.epa.gov/oppt/exposure/docs/episuitedl.htm ©2000 U.S. Environmental Protection Agency.

Other

B. Stability in Water

Test Substance

Identity: 2-Chloropyridine
Remarks: None

The computer modeling program can not estimate the rate constants for aqueous acid/base-catalyzed hydrolysis. Although hydrolysis cannot be predicted using a computer estimation model, 2-chloropyridine does not have a site in which the water molecule or hydroxide ion can displace an atom or group of atoms. Chemical hydrolysis at a pH normally found in the environment, i.e. 5 to 9, can be important for a variety of chemicals that have functional groups that are potentially hydrolysable, such as amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters. It is the position of Arch Chemicals that data for this endpoint is not necessary since this chemical does not possess a structure that is hydrolysable. The judgment is that 2-PCl would be resistant to acid/base-catalyzed hydrolysis.

C. Biodegradation – Entry 1 of 5

Test Substance

Identity:	2-Chloropyridine
Purity:	> 96%
Remarks:	Purchased from Sigma Chemical Co. St. Louis, MO

Method

Method:	Non-specific test method for substrate depletion and methane formation in a sealed system.
Test type:	Anaerobic biodegradation in a sediment/water slurry.
GLP:	Not stated
Year:	1994
Contact time:	12 months
Inoculum:	Sediment and ground water collected from a methanogenic aquifer contaminated with landfull leachate.
Remarks:	Experiments were performed in triplicate and employed both sterile and substrate-unamended controls. In addition acetate and 3-chlorobenzene were employed as positive controls. The headspace of the test vessels was monitored for methane formation by gas chromatography (GC). Methane produced in unamended controls was subtracted from that produced in substrate-amended vessels and compared to the theoretically expected amount based on Buswell's equation and the initial substrate concentration. Substrate depletion and metabolite formation was monitored by reverse-phase high-pressure liquid chromatography (HPLC).

Results

Degradation:	2-Chloropyridine was not removed from the test system and evidence of mineralization was not observed.
Results:	No methane production was observed. Substrate recovery after 1 year of incubation was 107±5%. No intermediates were observed.
Kinetic:	Not stated
Breakdown products:	Not stated
Remarks:	None

Conclusions The biodegradability of the test sub stance has been adequately characterized.

Data Quality

Reliability:	2A
Remarks:	Reliable with restrictions; acceptable, well-documented publication/study report which meets basic scientific principles.

Reference

Adrian, N. R. and Sulfita, J. M. 1994. Anaerobic biodegradation of halogenated and nonhalogenated N-, S- and O-heterocyclic compounds in aquifer slurries. Environ. Toxicol. Chem. 13, 1551-1557.

Other

Entry 2 of 5 for Biodegradation

Test Substance

Identity:	2-Chloropyridine
Purity:	Not stated
Remarks:	Purchased from Sigma Chemical Co. St. Louis, MO

Method

Method:	Non-specific test method for substrate depletion.
Test type:	Anaerobic
GLP:	Not stated
Year:	1995
Contact time:	12 months
Inoculum:	Sediment and ground water collected from a freshwater pond contaminated with small particles of asphalt.
Remarks:	Experiments were performed in duplicate and employed both sterile and substrate-unamended controls. Substrate depletion and metabolite formation was monitored by HPLC.

Results

Degradation:	2-Chloropyridine was not removed from the test system.
Results:	Some loss of 2-chloropyridine was observed; however, the loss was not significantly different from that in the corresponding sterile controls. No transformation was observed.
Kinetic:	Not stated
Breakdown products:	Not stated
Remarks:	None

Conclusions The biodegradability of the test sub stance has been adequately characterized.

Data Quality

Reliability:	2A
Remarks:	Reliable with restrictions; acceptable, well-documented publication/study report which meets basic scientific principles.

Reference Lui, S. M. 1995. Anaerobic dechlorination of chlorinated pyridines in anoxic freshwater sediment slurries. J. Environ. Sci. Health. A30, 485-503.

Other

Entry 3 of 5 for Biodegradation

Test Substance

Identity:	2-Chloropyridine
Purity:	Not stated
Remarks:	Purchased from Aldrich Chemical Co.

Method

Method:	Assessment of degradation based on substrate depletion.
Test type:	Anaerobic biodegradation
GLP:	Not stated
Year:	1989
Contact time:	200 days
Inoculum:	Sediment and overlying site water from an estuary.
Remarks:	Biodegradation of 2-chloropyridine was evaluated in sediment slurries (10% solids) under sulfate reducing conditions. Experiments were replicated and included control sediments. Testing was conducted at 78.8 μM. Test chambers were incubated in the dark at 23-25^{o}C. Samples for analysis were removed using a syringe and needle periodically. Substrate concentration was measured using HPLC.

Results

Degradation:	None reported
Results:	2-Chloropyridine was persistent in the anoxic sediment.
Kinetic:	Not stated
Breakdown products:	Not stated
Remarks:	None

Conclusions The biodegradability of the test sub stance has been adequately characterized.

Data Quality

Reliability:	2B
Remarks:	Reliable with restrictions; basis data given, comparable to guidelines/standards.

Reference Lui, S. M., Wu, C. H. and Huang, H. J. 1989. Toxicity and anaerobic biodegradability of pyridine and its derivatives under sulfidogenic conditions. Chemosphere 10, 2345-2357.

Other

Entry 4 of 5 for Biodegradation

Test Substance

Identity:	2-Chloropyridine
Purity:	Not stated
Remarks:	None

Method

Method:	Non-guideline specific study of biodegradation of the test substance in soil suspensions.
Test type:	Aerobic biodegradability
GLP:	No
Year:	1986
Contact time:	24 days
Inoculum:	Soil suspension
Remarks:	Degradation experiments were carried out in 500-ml Erlenmeyer flasks. Flasks were prepared to contain 150 ml of basas salts medium amended with yeast extract and potassium phosphate buffer adjusted to pH 7.0. To each replicate flask (note – replication noted in article, but the number of replicates was not specified) 1 ml of 2-chloropyridine solution was added to give a final substrate concentration of approximately 1 mM. Flasks were inoculated with 1 ml of a dilute soil suspension prepared by suspending 15 g soil (Fincastle silt loam) in 1 l of mineral salts medium and continuously stirring while 1-ml aliquots were removed. Flasks were incubated at 24^{o}C for up to 30 days. Subsamples were removed from each flask before and after inoculation and periodically throughout the incubation. 2-Chloropyridine concentrations were monitored by UV spectrophotometry during the incubation period. The disappearance of 2-chloropyridine from solutions plus the mineralization of pyridine-N was taken as evidence of degradation.

Results

Degradation:	UV analysis indicated a 47% loss of 2-chloropyridine from the test solutions by 24 days, while inorganic nitrogen released to the test solutions accounted for <1% degradation.
Results:	2-Chloropyridine did not appear to be appreciable degraded. The amount of 2-chloropyridine lost

	from the test solutions determined by UV analysis was 47% within 24 days. Less than 1% was determined to be biodegraded based on release of inorganic nitrogen in the test solutions, while 37% was lost through volatilization and 3.2% adsorbed by soil.
Kinetic:	Not stated
Breakdown products:	Not stated
Remarks:	None

Conclusions The biodegradability of the test sub stance has been adequately characterized.

Data Quality

Reliability:	2A
Remarks:	Reliable with restrictions; acceptable, well-documented publication/study report which meets basic scientific principles.

Reference Sims, G. K. and Sommers, L. E. 1986. Biodegradation of pyridine derivatives in soil suspensions. Environ. Toxicol. Chem. 3, 503-509.

Other

Entry 5 of 5 for Biodegradation

Test Substance

Identity:	2-Chloropyridine
Purity:	Not stated
Remarks:	None

Method

Method:	Non-specific method measuring substance depletion and inorganic N released.
Test type:	Aerobic biodegradation in soil
GLP:	Not stated
Year:	1985
Contact time:	64 days
Inoculum:	The test soil was a Fincast silt loam which had a pH of 6.7, organic carbon content of 12 g/kg, total N content of 1300 mg/kg, CEC of 0.15 mol (+)/kg and contained 0.25 kg H_2O/kg dry soil as – 0.03 MPa.
Remarks:	Test chambers were prepared in duplicate and dosed at 200 mmol/kg. At 3- and 4-day intervals the soils were adjusted for loss of moisture. After 0, 1, 2, 4, 8, 16, 32 and 64 days of incubation, the foam stoppers and soil from rjeplicate chambers were extracted and analyzed. In addition, a sterile treatment was extracted and analyzed after 7 days of incubation.

Results

Degradation:	89% of the test substance remained in the soil after 64 days of incubation, indicating little biodegradation of the test substance occurred over the study period. This was confirmed by little inorganic nitrogen accumulation during incubation.
Results:	The measured day 0 concentration of the test substance was 113.7% of the nominal concentration. After 64 days of incubation, 89% of the test substance remained in the soil. Accumulation of inorganic nitrogen at days 16, 32 and 64 was equivalent to 1.3, < 0.1 and <0.1% of the extratable test substance.
Kinetic:	Not stated
Breakdown products:	Not stated
Remarks:	None

Conclusions The biodegradability of the test sub stance has been adequately characterized.

Data Quality:

Reliability:	2A
Remarks:	Reliable with restrictions; acceptable, well-documented publication/study report which meets basic scientific principles.

Reference Sims, G. K. and Sommers, L. E. 1985. Degradation of pyridine derivatives in soil: Chemical and biological assessment. J. Environ. Qual. 14, 580-584.

Other

D. Transport between Environmental Compartments (Fugacity)

Test Substance

Identity:	2-Chloropyridine
Remarks:	None

Method

Method:	Estimation
Model:	Level III Fugacity Model
Remarks:	None

Results

Estimated distribution and media concentration:		Mass Amount (%)	Half-Life (hr)	Emissions (kg/hr)
	Air	7.52	986	1000
	Water	48.8	900	1000
	Soil	43.6	900	1000
	Sediment	0.104	3.6×10^3	0
Remarks:	Physical chemical values utilized in this model were default values obtained from the EPIWIN program.			

Reference Level III Fugacity Model. (EPI Suite™ v.3.10). Downloadable at http://www.epa.gov/oppt/exposure/docs/episuitedl.htm ©2000 U.S. Environmental Protection Agency.

Other

IV. Ecotoxicity

A. Acute Toxicity to Fish

Test Substance

Identity:	2-Chloropyridine
Remarks:	None

Method

Method:	Estimation
Test type:	96-hour LC_{50}
Organism:	Fish
Remarks:	None

Results

LC_{50} (96 hours):	277 mg/l
Remarks:	None

Reference

Nabholz, J. V., Cash, G., Meylan, W. M. and Howard, P. H. 2001. ECOSAR: A Computer Program for Estimating the Ecotoxicity of Industrial Chemicals Based on Structure Activity Relationships, Version 0.99g. Washington, DC: Risk Assessment Division, Office of Pollution Prevention and Toxics, United States Environmental Protection Agency. Available from EPA web page at http://www.epa.gov/oppt/newchems/21ecosar.htm or http://www.epa.gov/oppt/exposure/docs/episuitedl.htm

Other

B. Acute Toxicity to Daphnids

Test Substance

Identity:	2-Chloropyridine
Remarks:	None

Method

Method:	Estimation
Test type:	48-hour LC_{50}
Organism:	Daphnid
Remarks:	None

Results

LC_{50} (48 hours):	286 mg/l
Remarks:	None

Reference

Nabholz, J. V., Cash, G., Meylan, W. M. and Howard, P. H. 2001. ECOSAR: A Computer Program for Estimating the Ecotoxicity of Industrial Chemicals Based on Structure Activity Relationships, Version 0.99g. Washington, DC: Risk Assessment Division, Office of Pollution Prevention and Toxics, United States Environmental Protection Agency. Available from EPA web page at http://www.epa.gov/oppt/newchems/21ecosar.htm or http://www.epa.gov/oppt/exposure/docs/episuitedl.htm

Other

C. Acute Toxicity to Aquatic Plants

Test Substance

Identity:	2-Chloropyridine
Remarks:	None

Method

Method:	Estimation
Test type:	96-hour EC_{50}
Organism:	Green Algae
Remarks:	None

Results

EC_{50} (96 hours):	173 mg/l
Remarks:	None

Reference

Nabholz, J. V., Cash, G., Meylan, W. M. and Howard, P. H. 2001. ECOSAR: A Computer Program for Estimating the Ecotoxicity of Industrial Chemicals Based on Structure Activity Relationships, Version 0.99g. Washington, DC: Risk Assessment Division, Office of Pollution Prevention and Toxics, United States Environmental Protection Agency. Available from EPA web page at http://www.epa.gov/oppt/newchems/21ecosar.htm or http://www.epa.gov/oppt/exposure/docs/episuitedl.htm

Other

V. Mammalian Toxicity

A. Acute Toxicity – Entry 1 of 5

Test Substance

Identity:	2-Chloropyridine
Purity:	Not determined
Remarks:	None

Method

Method:	Not stated
Type:	LD_{50}
GLP:	No
Year:	1964
Species/Strain:	Rat/Manor Wistar
Sex:	Male
Number of animals/ sex/dose:	6
Vehicle:	Methylcellulose
Route of administration:	Oral (gavage)
Remarks:	Groups of 6 male rats were administered a single dose of the test substance suspended in a 0.5% aqueous dispersion of methylcellulose via oral gavage at concentrations of 100, 215, 464, 681, 1000, 1470 and 2150 mg/kg. Each dose level was prepared in a concentration that enabled the delivery of a constant volume of 1.0 ml/100 g of body weight. Rats were in the weight range of 201-304 g. Food was withheld from all ras for 16 hours prior to dosing. Food and water were available *ad libitum* at all other times. Rats were observed for signs of toxicity and mortality continuously for 4 hours post-dose, at 24 hours post dose and once daily thereafter for 13 days. At the termination of the 14-day observation period, surviving rats were sacrificed. Necropsies were performed on all rats.

Results

Value: LD_{50} – 342 mg/kg (confidence limits – 211 – 558 mg/kg)

Mortality rate:

Dose (mg/kg)	Mortality
100	0/6
215	1/6
464	5/6
681	6/6
1000	6/6

1470	6/6
2150	6/6

Remarks: At 16 hours post-dose, 4 rats in the 100 mg/kg dose group exhibited nasal porphyrin. At 24 hours post-dose, 4 rats appeared hypoactive. All animals appeared normal thereafter until study termination. Two rats in the 215 mg/kg dose group exhibited nasal porphyrin discharge at 4 hours post-dose. At 24 hours post-dose 4 rats were ataxic, sedate, hypoactive and displayed nasal porphyrin discharge. At 2 days all rats were hypoactive and continued to demonstrate nasal discharge. One animal was found dead on day 3. The remaining rats appeared normal throughout the remainder of the observation period. Within 6 hours 5 rats from the 464 mg/kg dose group exhibited ataxia and hypoactivity. One rat became prostrate. At 24 hours all rats were ataxic and exhibited nasal porphyrin. One rat was prostrate and dyspneic. At 2 days 1 rat died and 2 were ataxic and the remaining 3 appeared hypoactive. At 3 days all 5 rats were hypoactive and appeared depressed. At 4 days one died and the remaining 4 continued to be hypoactive and became hypersensitive to touch. Two more rats died on days 5 and 6. The remaining 2 rats were hypoactive and hypersensitive to touch. A fifth rat died. The remaining rat recovered and appeared normal from days 9 through 14. rats in the 681, 1000, 1470 and 2150 mg/kg dose groups displayed hypotonia, ataxia, sedation, hypnosis, loss of righting reflex, pinna and placing reflexes, bradypnea, dyspnea, cyanosis, ptosis, salivation and reduced pain responses within 2 to 18 hours post-dose. Rats in all dose groups except the 681 mg/kg dose group died within 2 to 4 hours post-dose. Rats in the 681 mg/kg dose group died within 3 days. At necropsy, 1 rat in the 100 mg/kg dose group had hydronephrosis. The rat that died in the 215 mg/kg dose group exhibited a pale liver with friable accentuated lobules and the lungs were congested. Necropsy findings in the rats that died in the 464 mg/kg dose group included congested lungs, congested liver, hemorrhages of the stomach, small intestines and urinary bladder and icterus. All rats in the 100, 215 andf 464 mg/kg dose groups that

survived to the 14-day post-exposure period had essentially normal necropsy findings. Necropsy findings in the 681, 1000, 1470 and 2150 mg/kg dose groups included scrotal erythema, hemorrhages of the stomach, intestines and urinary bladder and congested lungs and liver. Hydronephrosis (unilateral and bilateral) was scattered in all groups.

Conclusions

Remarks: The acute oral LD_{50} has been adequately characterized.

Data Quality

Reliability: 1B

Remarks: Reliable without restriction; comparable to guideline study.

Reference

Wazeter, F. X. 1964. Acute Toxicity Studies in Rats and Rabbits. Report # 122-003. International Research and Development Corporation, Mattawan, MI.

Other

Acute Toxicity – Entry 2 of 5

Test Substance

Identity:	2-Chloropyridine
Purity:	> 97%
Remarks:	None

Method

Method:	"Sleeve" technique described by Draize et al. (1944) and Rowe et al. (1952). These references are cited in the study reference.
Type:	LD_{50}
GLP:	No
Year:	1966
Species/Strain:	Rabbit
Sex:	Male and female
Number of animals/ dose:	4-5
Vehicle:	None
Route of administration:	Dermal
Remarks:	Groups of male and female rabbits, weighing 1.3 to 2.3 kg, were exposed to the undiluted test substance dermally at concentratins of 40, 48, 50, 58, 63, 68, 79, 82 or 100 mg/kg.

Results

Value: LD_{50} – 64 mg/kg (confidence limits – 55.5 to 73.5 mg/kg)

Mortality rate:

Dose (mg/kg)	Mortality
40	0/5
48	1/4
50	1/5
58	2/5
63	3/4
68	2/5
79	3/4
82	3/5
100	5/5

Remarks: The test substance caused only transient local congestion of the skin when applied to either intact or abraded skin. The primary gross lesion observed was hemorrhagic necrosis of the liver.

Conclusions

Remarks: The acute dermal LD_{50} has been adequately characterized.

Data Quality

Reliability: 2A

Remarks: Reliable with restriction; acceptable, well-documented publication which meets basic scientific principles.

Reference

Gehring, P. J., Torkelson, T. R. and Oyen, F. 1967. A Comparison of the Lethality of Chlorinated Pyridines and a Study of the Acute Toxicity of 2-Chloropyridine. Toxicol. Appl. Pharmacol. 11, 361-371.

Other

Acute Toxicity – Entry 3 of 5

Test Substance

Identity:	2-Chloropyridine
Purity:	Not determined
Remarks:	None

Method

Method:	Not stated
Type:	Acute dermal toxicity
GLP:	No
Year:	1964
Species/Strain:	Rabbit
Sex:	Male and female
Number of animals/ sex/dose:	3
Vehicle:	None
Route of administration:	Dermal
Remarks:	Six rabbits (3 M; 3 F) per group, weighing between 2040 and 2828 g, were administered a single dose of the undiluted test substance dermally at concentrations of 200 and 2000 mg/kg. The back of each rabbit was clipped. The clipped back of 3 rabbits per group was abraded and the skin of the remaining 3 rabbits was left intact. The rabbits were exposed to the test substance for a period of 24 hours. The dosing site was not occluded during the 24 hour exposure period. Rabbits were observed frequently for pharmacotoxic effects during the first 4 hours after application, at 24 hours and once daily thereafter for a total of 14 days. The degree of dermal irritation and damage was evaluated. At the end of the observation period all surviving rabbits were weighed, sacrificed and necropsied. Rabbits that did not survive the observation period also were necropsied.

Results

Value:	LD_{50} – < 200 mg/kg
Mortality rate:	200 mg/kg – 5/6 2000 mg/kg – 6/6
Remarks:	Five rabbits in the 200 mg/kg dose group died within 18 to 40 hours post-dose. Death was preceded by cyanosis, bradypnea and dyspnea,

lacrimation, hypothermia and hypotonia of the sleletal musculature. One rabbit with intact skin survived. This rabbit demonstrated a very slight erythema of the area of application for the entire observation period. All rabbits in the 2000 mg/kg dose group died within 18 hours after displaying signs as noted above. Necropsy findings in the 200 mg/kg dose group included excessive mucous in the stomach and lungs that failed to collapse and which were congested and hemorrhagic. Fluid was found in the thoracic cavity and a strong odor of the test substance was present in the thoracic cavity. One rabbit displayed a hemorrhagic cecum. The surviving rabbit in this group exhibited no gross lesions. Necropsy findings in the 2000 mg/kg dose group included excessive mucous in the stomach and lungs that failed to collapse and which were congested and hemorrhagic. Foam was present in the trachea and major bronchi. A strong test substance odor was present in the thoracic cavity of all rabbits.

Conclusions

Remarks: The acute dermal toxicity has been adequately characterized.

Data Quality

Reliability: 1B

Remarks: Reliable without restriction; comparable to guideline study.

Reference

Wazeter, F. X. 1964. Acute Toxicity Studies in Rats and Rabbits. Report # 122-003. International Research and Development Corporation, Mattawan, MI.

Other

Acute Toxicity – Entry 4 of 5

Test Substance

Identity:	2-Chloropyridine
Purity:	> 97%
Remarks:	None

Method

Method:	Not stated
Type:	Acute inhalation toxicity
GLP:	No
Year:	1966
Species/Strain:	Rat
Sex:	Female
Number of animals/ dose:	10-20
Vehicle:	None
Route of administration:	Inhalation
Remarks:	Groups of female rats, approximately 10 weeks old and weighing 132 to 190 g, were exposed to the test substance via inhalation at concentrations of 50, 100, 250, 500 and 1000 ppm for 0.1 to 7.0 hours. The concentration of 2-chloropyridine was monitored continuously during the exposure by infrared spectrophotometry. The degree and character of organic damage resulting from exposure to the test substance were the presence of gross pathologic or histopathologic lesions, hematologic alterations, organ weight changes and changes in the blood chemistry. Liver, kidney, spleen, heart, lungs and brain were examined for weight changes and together with pancreas and adrenals for the presence of histologic lesions. Hematologic studies consisted of erythrocyte, leukocyte and differential counts and hematocrit and hemoglobin determinations. Parameters used to detect changes in blood chemistry were blood urea nitrogen, serum glutamic-pyruvic transaminase and serum glutamic-oxalacetic transaminase. Rats were observed for 2 weeks post-exposure.

Results

Value:	LC_{50} – > 100 ppm but < 250 ppm

Mortality rate:

Dose Level (ppm)	Length of Exposure (hrs)	Mortality Rate
50	7.0	0/10
	4.0	0/10
100	7.0	13/20
	4.0	7/20
	2.0	0/10
250	7.0	12/12
	4.0	14/20
	2.0	8/10
	1.0	2/10
	0.5	0/10
500	2.0	15/15
	1.0	8/15
	0.5	2/15
	0.2	0/14
1000	1.0	14/15
	0.5	8/10
	0.2	8/17
	0.1	0/20

Remarks: The concentration of 2-chloropyridine vapor was within 7% of the desired concentration throughout the exposure period. Liver damage was the primary alteration caused by the inhalation of the test article. Histopathologic examinations revealed that the test substance caused central lobular necrosis, hemorrhage and fatty degeneration as well as cellular infiltration. The extent and type of damage varied with the exposure. Maximum single-dose exposures not causing these changes were 100 ppm for 3 minutes, 50 ppm for 6 minutes, 25 ppm for 12 minutes and 10 ppm for 30 minutes. Maximum single-dose exposures that did not cause death 1000 ppm for 6 minutes, 500 ppm for 12 minutes, 250 ppm for 30 minutes, 100 ppm for 2 hours and 50 ppm for 4 hours.

Conclusions

Remarks: The LC_{50} was not calculated, but based on the available data, the 4-hour LC_{50} is between 100 and

250 ppm. Therefore, the acute inhalation LC_{50} has been adequately characterized.

Data Quality

Reliability: 2A

Remarks: Reliable with restriction; acceptable, well-documented publication which meets basic scientific principles.

Reference

Gehring, P. J., Torkelson, T. R. and Oyen, F. 1967. A Comparison of the Lethality of Chlorinated Pyridines and a Study of the Acute Toxicity of 2-Chloropyridine. Toxicol. Appl. Pharmacol. 11, 361-371.

Other

Acute Toxicity – Entry 5 of 5

Test Substance

Identity:	2-Chloropyridine
Purity:	Not determined
Remarks:	None

Method

Method:	Not stated
Type:	Acute inhalation toxicity
GLP:	No
Year:	1964
Species/Strain:	Rat
Sex:	Male
Number of animals/ sex/dose:	10
Vehicle:	None
Route of administration:	Inhalation
Remarks:	Ten male albino rats, weighing 235 to 270 g, were exposed to the test substance via inhalation at a concentration of approximately 6.05 mg/l for 6 hours. The exposure was conducted in a 354 l stainless steel chamber. The total airflow through the system was 49±1 liters/minute. Food and water were available *ad libitum*, except during the period of exposure. During exposure, rats were observed for signs of toxicity and mortality continuously for 1 hour and at ½ hour intervals thereafter until the end of the exposure period. After the exposure period, the rats were observed daily for 14 days. A necropsy was performed on all rats.

Results

Value:	LC_{50} – < 6.05 mg/l
Mortality rate:	10/10
Remarks:	All animals died within 3 days after exposure. Observations during exposure included hypoactivity, sedation and ataxia. At the end of 4 hours of exposure, all rats were prostrate. Three rats exhibited dyspnea. Three rats died between 4 and 6 hours of the exposure period. At the end of 6 hours the surviving rats were prostrate, comatose and dyspneic. Within 24 hours, 2 additional rats died. The remaining 5 rats were still prostrate and comatose. Clear ocular discharge was noted.

Within the following 24-hour period after exposure, 4 more rats died. The tenth rat died at 3 days post exposure. Necropsy findings in all rats included congestion of the lungs and liver, slight congestion of the small intestines, blood in the abdominal cavity and /or severe hemorrhages of the stomach, small intestines and urinary bladder.

Conclusions

Remarks: The acute inhalation toxicity has been partially characterized. These data support the data of Gehring et al. (1967).

Data Quality

Reliability: 1B

Remarks: Reliable without restriction; comparable to guideline study.

Reference

Wazeter, F. X. 1964. Acute Toxicity Studies in Rats and Rabbits. Report # 122-003. International Research and Development Corporation, Mattawan, MI.

Other

B. Genetic Toxicity *In Vitro*– Entry 1 of 3

Test Substance

Identity:	2-Chloropyridine
Purity:	99%
Remarks:	None

Method

Method:	Ames/*Salmonella* Bacterial Point Mutation Assay
Type:	Reverse mutation assay
Test system:	Bacteria
GLP:	Not stated
Year:	1987
Species/Strain:	*Salmonella typhimurium*/TA97, TA98, TA100 and TA102
Metabolic activation:	9000 g (S9) liver homogenate from Arochlor 1254-induced male Sprague-Dawley rats.
Concentrations tested:	50, 100, 500, 1000 and 5000 µg/plate without S9 50, 100, 500, 1000, 5000 and 7500 µg/plate with S9
Statistical methods:	Stead et al. (1981) and Bernstein et al. (1982) from the reference list in the cited study.
Remarks:	The test procedures were the same as initially described by Ames et al. (1975) (in reference list of cited study). All assays were conducted in the standard plate incorporation assay on at least 2 separate days both with and without metabolic activation. The test substance was tested at 6 concentrations in duplicate. Appropriate negative (solvent) and positive controls were run in parallel with the assay. The test substance and solvent control were dissolved in dimethyl sulfoxide (DMSO). The test substance was not designated positive or negative unless reproducible results were obtained. A positive response was defined as a reproducible, concentration-related increase in histidine independent revertants over the solvent control concentration in at least one strain/activation combination. A definitive positive or negative result was assigned to a test result when the statistical methods and visual examination of the data agreed. An equivocal response occurred when 1) test results were not reproducible, 2) a low-level, but not concentration-related, increase in *his+* colonies was obtained or 3) when an increase was observed at only 1 concentration level.

Results

Result:	2-Chloropyridine elicited a mutagenic response in all 4 *Salmonella* strains in the presence of the metabolic activation system only. No toxicity was observed at any concentration.
Cytotoxic Concentration:	None
Genotoxic effects:	Negative without metabolic activation. Positive with metabolic activation in all tester strains.
Statistical results:	Not stated
Remarks:	None

Conclusions

Remarks:	This endpoint has been adequately characterized.

Data Quality

Reliability:	1B
Remarks:	Reliable without restriction; comparable to guideline study.

Reference

Claxton, L. D., Dearfield, K. L., Spanggord, R. J., Riccio, E. S. and Mortelmans, K. 1987. Comparative mutagenicity of halogenated pyridines in the *Salmonella typhimurium*/mammalian microsome test. Mutat. Res. 176, 185-198.

Other

Genetic Toxicity *In Vitro*– Entry 2 of 3

Test Substance

Identity:	2-Chloropyridine
Purity:	Not stated
Remarks:	None

Method

Method:	Not stated
Type:	Mammalian cell forward mutation assay
Test system:	Mammalian cells
GLP:	Not stated
Year:	1992
Cell type:	Heterozygous L5178Y $TK^{+/-}$ -3.7.2C mouse lymphoma cells.
Metabolic activation:	S9 homogenate derived from livers of Arochlor-induced rats.
Concentrations tested:	Ranging from 1200-2004 µg/ml without S9 activation. Ranging from 400-1100 µg/ml with S9 activation
Statistical methods:	Not stated
Remarks:	Duplicate cultures of L5178/$TK^{+/-}$ -3.7.2C cells were treated with or without metabolic activation for 4 hours according to the procedures described by Turner et al. (1984)(in reference list of cited study). The mutagenicity assay was performed according to the procedures described by Doerr et al. (1989) (in reference list of cited study). A positive response was defined as one in which the induced mutant frequency was $>70x10^{-6}$, at concentrations yielding >10% relative total growth. Equivocal responses were those that gave approximately equal evidence of positive and negative responses. The positive control compounds were ethyl methanesulfonate (without S9) and benzo[*a*]pyrene (with S9).

Results

Result:	In the absence of metabolic activation, 2-chloropyridine induced small increases in the mutant frequencies. In the presence of the metabolic activation system, the test substance greatly increased the frequency of gene mutations.

The test substance induced both small and large colony tk mutants.

Cytotoxic Concentration:	None
Genotoxic effects:	Positive
Statistical results:	Not stated
Remarks:	An analysis of the relative small and large colony tk mutant frequencies was not performed because the induced response was not sufficient to allow interpretation of the data. Colony sizing was performed on the positive control cultures. Colony sizing analysis for the positive controls demonstrated the ability to recover and quantitate both classes of tk mutants.

Conclusions

Remarks:	This endpoint has been adequately characterized.

Data Quality

Reliability:	2A
Remarks:	Reliable with restriction; acceptable, well-documented publication which meets basic scientific principles.

Reference

Dearfield, K. L., Harington-Brock, D., Doerr, D. L., Parker, L. and Moore, M. M. 1993. Genotoxicity of three pyridine compounds to L5178Y mouse lymphoma cells. Mutat. Res. 301, 57-63.

Other

Genetic Toxicity *In Vitro*– Entry 3 of 3

Test Substance

Identity:	2-Chloropyridine
Purity:	Not stated
Remarks:	None

Method

Method:	Not stated
Type:	Mammalian cell chromosome aberrations and micronuclei
Test system:	Mammalian cells
GLP:	Not stated
Year:	1992
Cell type:	Heterozygous L5178Y $TK^{+/-}$ -3.7.2C mouse lymphoma cells.
Metabolic activation:	S9 homogenate derived from livers of Arochlor-induced rats.
Concentrations tested:	Ranging from 1920-1992 µg/ml without S9 activation. Ranging from 500-1100 µg/ml with S9 activation
Statistical methods:	Not stated
Remarks:	Duplicate cultures of L5178/$TK^{+/-}$ -3.7.2C cells were treated with or without metabolic activation for 4 hours according to the procedures described by Turner et al. (1984)(in reference list of cited study). The cytogenetic analysis was performed according to the procedures described by Doerr et al. (1989) (in reference list of cited study). For the cytogenetic endpoints a positive call is based upon meeting 2 criteria: The response was double the negative control for not only the experiment but also the periodically updated historic means for negative controls. Positive control cultures were analyzed for cytogenetic endpoints only for those compounds that demonstrated a very weak or equivocal response in the mutagenesis assay. The positive control compound was ethyl methanesulfonate (without S9).

Results

Result:	In the absence of metabolic activation, the test substance induced a small increase in the frequency of chromosome aberrations. In the presence of metabolic activation, it significantly increased the frequency of chromosome aberrations. The test substance significantly increased the number of micronuclei with and without metabolic activation.
Cytotoxic Concentration:	None
Genotoxic effects:	Positive
Statistical results:	Not stated
Remarks:	An analysis of the relative small and large colony tk mutant frequencies was not perfo rmed because the induced response was not sufficient to allow interpretation of the data. Colony sizing was performed on the positive control cultures. Colony sizing analysis for the positive controls demonstrated the ability to recover and quantitate both classes of tk mutants.

Conclusions

Remarks:	This endpoint has been adequately characterized.

Data Quality

Reliability:	2A
Remarks:	Reliable with restriction; acceptable, well-documented publication which meets basic scientific principles.

Reference

Dearfield, K. L., Harington-Brock, D., Doerr, D. L., Parker, L. and Moore, M. M. 1993. Genotoxicity of three pyridine compounds to L5178Y mouse lymphoma cells. Mutat. Res. 301, 57-63.

Other